General

Guideline Title

Medical management of ectopic pregnancy.

Bibliographic Source(s)

American College of Obstetricians and Gynecologists (ACOG). Medical management of ectopic pregnancy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Jun. 7 p. (ACOG practice bulletin; no. 94). [29 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American College of Obstetricians and Gynecologists (ACOG). Medical management of tubal pregnancy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 1998 Dec. 7 p. (ACOG practice bulletin; no. 3).

The American College of Obstetricians and Gynecologists (ACOG) reaffirmed the currency of this guideline in 2012.

Recommendations

Major Recommendations

The grades of evidence (I-III) and levels of recommendations (A-C) are defined at the end of "Major Recommendations" field.

The following conclusion is based on good and consistent evidence (Level A):

> In comparing systemic methotrexate with tube-sparing laparoscopic surgery, randomized trials have shown no difference in overall tubal preservation, tubal patency, repeat ectopic pregnancy, or future pregnancies.

The following recommendations and conclusions are based on limited or inconsistent evidence (Level B):

> An increase in serum human chorionic gonadotropin (hCG) of less than 53% in 48 hours confirms an abnormal pregnancy.
> With an hCG level of 5,000 mIU/mL or higher, multiple doses of methotrexate may be appropriate.
> Methotrexate can be considered in those women with a confirmed, or high clinical suspicion of, ectopic pregnancy who are hemodynamically stable with an unruptured mass.
> Failure of the hCG level to decrease by at least 15% from day 4 to day 7 after methotrexate administration is considered treatment failure requiring therapy with either additional methotrexate administration or surgical intervention.
> Post-treatment hCG levels should be monitored until a nonpregnancy level is reached.

The following conclusion is based primarily on consensus and expert opinion (Level C):

If the initial hCG level is less than 200 mU/mL, 88% of patients experience spontaneous resolution.

Definitions:

Grades of Evidence

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Recommendations

Level A — Recommendations are based on good and consistent scientific evidence.

Level B — Recommendations are based on limited or inconsistent scientific evidence.

Level C — Recommendations are based primarily on consensus and expert opinion.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Tubal ectopic pregnancy

Guideline Category

Counseling

Diagnosis

Management

Treatment

Clinical Specialty

Obstetrics and Gynecology

Intended Users

Physicians

Guideline Objective(s)

- To aid practitioners in making decisions about appropriate obstetric and gynecologic care
- To review the risks and benefits of the use of methotrexate in the management of ectopic pregnancy

Target Population

Pregnant women presenting with signs and symptoms of ectopic pregnancy

Interventions and Practices Considered

Diagnosis

- Clinical signs, physical symptoms
- Serial human chorionic gonadotropin (hCG) levels
- Transvaginal ultrasonography
- Serum progesterone levels

Management/Treatment

- Determining if a patient is a candidate for methotrexate therapy
- Methotrexate
  - Single-dose regimen protocol
  - Two-dose regimen protocol
  - Fixed multidose regimen protocol
- Surveillance after methotrexate therapy
  - Serial hCG levels
- Patient counseling and education concerning side effects of methotrexate
- Expectant management of ectopic pregnancy

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Incidence of heterotopic pregnancy
- Success rate of methotrexate regimen
- Methotrexate-associated morbidity
- Tubal preservation
- Tubal patency
- Repeat ectopic pregnancy
- Future pregnancies
- Patient satisfaction

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

2008 Original Guideline

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' (ACOG's) own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and May 2007. The search was restricted to articles published in the English language. Priority was given to the articles reporting results of original research although review articles and commentaries also were consulted. Abstracts of research presented at symposiums and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles.

2012 Reaffirmation

The NCBI database was searched from 2008 to 2012. Committee members conducted a literature search with the assistance from the ACOG Resource Center staff who routinely perform the Practice Bulletin literature searches.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force.

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

2008 Original Guideline

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician-gynecologists were used. See also the "Rating Scheme for the Strength of Recommendations" field regarding Grade C recommendations.

2012 Reaffirmation

The Committee on Practice Bulletins - Gynecology met in September 2012 and reaffirmed this document. A committee member reviewed the document and new literature on the topic. The document was then reviewed by the committee and the committee agreed that it is current and accurate.

Rating Scheme for the Strength of the Recommendations

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A — Recommendations are based on good and consistent scientific evidence.

Level B — Recommendations are based on limited or inconsistent scientific evidence.

Level C — Recommendations are based primarily on consensus and expert opinion.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive Board.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improved treatment of tubal ectopic pregnancies with methotrexate

Potential Harms

Adverse Effects Associated with Methotrexate Treatment

Because methotrexate affects all rapidly dividing tissues within the body, including bone marrow, the gastrointestinal mucosa, and the respiratory epithelium, it should not be given to women with blood dyscrasias or active gastrointestinal and respiratory disease.
Methotrexate is directly toxic to the hepatocytes and is cleared from the body by renal excretion; therefore, it should not be used in women with liver or kidney disease.
Methotrexate morbidity usually is dose and treatment duration dependent. Because methotrexate affects rapidly dividing tissues, gastrointestinal side effects, such as nausea, vomiting, and stomatitis, are the most common. Therefore, women treated with methotrexate should be advised not to use alcohol and nonsteroidal anti-inflammatory drugs (NSAIDs). Elevation of liver enzymes usually is seen only with multidose regimens and resolves after discontinuing methotrexate use or increasing the rescue dose of folinic acid. Alopecia is a rare side effect with the doses used to treat ectopic pregnancy.
It is not unusual for women treated with methotrexate to experience abdominal pain 2–3 days after administration, presumably from the cytotoxic effect of the drug on the trophoblast tissue, causing tubal abortion.

Contraindications

Contraindications

Absolute Contraindications to Methotrexate Therapy

Breastfeeding
Overt or laboratory evidence of immunodeficiency
Alcoholism, alcoholic liver disease, or other chronic liver disease
Preexisting blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia
Known sensitivity to methotrexate
Active pulmonary disease
Peptic ulcer disease
Hepatic, renal, or hematologic dysfunction

Relative Contraindications to Methotrexate Therapy

Gestational sac larger than 3.5 cm
Embryonic cardiac motion

Qualifying Statements

Qualifying Statements

These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1998 Dec (revised 2008 Jun; reaffirmed 2012)

Guideline Developer(s)

American College of Obstetricians and Gynecologists - Medical Specialty Society

Source(s) of Funding

American College of Obstetricians and Gynecologists (ACOG)

Guideline Committee

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins- Gynecology

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Not stated

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Guideline Availability

Electronic copies: None available

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 933104, Atlanta, GA 31193-3104; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site .

Availability of Companion Documents

Proposed performance measures are included in the original guideline document.

Patient Resources

The following is available:

- Ectopic pregnancy. Atlanta (GA): American College of Obstetricians and Gynecologists (ACOG); 2002.

Electronic copies: Available from the American College of Obstetricians and Gynecologists (ACOG) Web site . Copies are also available in Spanish.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 933104, Atlanta, GA 31193-3104; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on January 14, 2005. This summary was updated by ECRI Institute on July 29, 2008. The updated information was verified by the guideline developer on August 20, 2008. The currency of the guideline was reaffirmed by the developer in 2012 and this summary was updated by ECRI Institute on March 7, 2014.

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